#7

PATENT

CERTIFICATE OF MAILING

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Jane A. Walker — April 3, 2003 Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Achilefu et al.
Serial No.:	09/757,332
Filing Date:	January 9, 2001
Group Art Unit:	1619
Confirmation No.:	5505
Title:	**HYDROPHILIC CYANINE DYES**
Atty Docket No.:	MRD-66

Cincinnati, Ohio 45202 April 3, 2003

Box SEQUENCE
P.O. Box 2327
Arlington, VA 22202

STATEMENT UNDER 37 C.F.R. §1.821(e & f)

The substitute paper copy of the "Sequence Listing" submitted herewith for consideration in the above-referenced application and the computer readable copy of that sequence listing submitted herewith are identical.

Respectfully submitted,

WOOD, HERRON & EVANS, L.L.P.

Beverly A. Lyman

Beverly A. Lyman, Ph.D.
Reg. No. 41,961

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(513) 421-7269 (facsimile)
K:\MRD\66\STATE sequence compliance.wpd

0590
0305

BIOTECHNOLOGY SYSTEMS BRANCH

RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/757,332
Source: OIPE
Date Processed by STIC: 2/27/2003

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:
1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.
PATENTIN 2.1 e-mail help: patin21help@uspto.gov or phone 703-306-4119 (R. Wax)
PATENTIN 3.0 e-mail help: patin3help@uspto.gov or phone 703-306-4119 (R. Wax)

TO **REDUCE** ERRORED SEQUENCE LISTINGS, **PLEASE** USE THE **CHECKER VERSION 3.1 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:
http://www.uspto.gov/web/offices/pac/checker

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202
3. **Hand Carry directly to:**
   U.S. Patent and Trademark Office, Technology Center 1600, Reception Area, 7th Floor, Examiner Name, Sequence Information, Crystal Mall One, 1911 South Clark Street, Arlington, VA 22202
   Or
   U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202
4. **Federal Express, United Parcel Service, or other delivery service to:** U.S. Patent and Trademark Office, Box Sequence, Room 1B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 01/29/2002

Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: 09/757,332

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1	Wrapped Nucleics Wrapped Aminos	The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."
2	Invalid Line Length	The rules require that a line not exceed 72 characters in length. This includes white spaces.
3	Misaligned Amino Numbering	The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.
4	Non-ASCII	The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.
5	Variable Length	Sequence(s)____contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
6	PatentIn 2.0 "bug"	A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.
7	Skipped Sequences (OLD RULES)	Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence: (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.
8	Skipped Sequences (NEW RULES)	Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence. <210> sequence id number <400> sequence id number 000
9	Use of n's or Xaa's (NEW RULES)	Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.
10 ✓	Invalid <213> Response	Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence
11 ✓	Use of <220>	Sequence(s) 1-8 missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown.". Please explain source of genetic material in <220> to <223> section. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
12	PatentIn 2.0 "bug"	Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
13	Misuse of n	n can only be used to represent a single nucleotide in a nucleic acid sequence. N is not used to represent any value not specifically a nucleotide.

delete ALL alphabetical designs. Use only numeric identifiers in new Sequence Rules format

09/757,332 1

delete

~~SEQUENCE LISTING~~

delete

<110> ~~APPLICANT:~~ Samuel I. Achilefu
Raghavan Rajagopalan
Richard B. Dorshow
Joseph E. Bugaj
delete ~~ASSIGNEE:~~ Mallinckrodt Inc.

pp 1-3
Does No: Comply
Corrected Diskette Needed

<120> ~~TITLE:~~ Hydrophilic Cyanine Dyes

<130> ~~DOCKET/FILE REFERENCE~~: MRD-66 → <1407 <1417 insert these mandatory numeric identifiers and responses

<150> ~~PRIOR APPLICATION NUMBER:~~ US 09/484,319
<151> ~~FILING DATE~~: 2000-01-18

<160> ~~NUMBER OF SEQUENCES:~~ 8

<170> ~~SOFTWARE:~~ FastSEQ for Windows Version 3.0

<210> ~~SEQ ID NO:~~ 1
<211> ~~LENGTH~~: 8
<212> ~~TYPE:~~ PRT
<213> ~~ORGANISM~~ Synthetic invalid response - see items 10 and 11 on Error Summary Sheet
<2207 → insert this mandatory numeric identifier wherever <2217, <2222, or <2237 is shown
<221> MOD_RES
<222> (1)..(0) delete delete

<223> Xaa = D-Phe → <2217 MOD_RES <2227 (2), (7) <2237

These don't exist per sequence rules

<224> ~~Xbb~~ Xaa = Cys with an intramolecular disulfide bond between two Cys amino acids

<225> ~~Xcc~~ Xaa = D-Trp → <2217 MOD_RES <2227 (4) <2237

<400> ~~SEQ ID NO:~~ 1
Xaa Xbb Tyr Xcc Lys Thr Xbb Thr
1 5

These are invalid. Use Xaa at all times

<210> ~~SEQ ID NO:~~ 2
<211> ~~LENGTH~~: 8
<212> ~~TYPE~~: PRT
<213> ~~ORGANISM:~~ Synthetic → <2207 mandatory
<221> MOD_RES
<222> (1)..(0) delete

<223> Xaa = D-Phe → <2217 MOD_RES <2227 (2), (7) <2237

<224> ~~Xaa Xbb~~ = Cys with an intramolecular disulfide bond between two Cys amino acids

<225> ~~Xaa Xcc~~ = D-Trp → <2217 MOD_RES <2227 (4) <2237

<226> ~~Xdd~~ = Thr-OH → <2217 MOD_RES <2227 (8) <2237

<400> ~~SEQ ID NO:~~ 2
Xaa Xbb Tyr Xcc Lys Thr Xbb Xdd
1 5
invalid

<210> ~~SEQ ID NO:~~ 3
<211> ~~LENGTH~~: 11

<212> ~~TYPE:~~ PRT
<213> ~~ORGANISM:~~ Synthetic

→ <2207

<221> MOD_RES
<222> (1)...(0) delete

<400> ~~SEQ ID NO:~~ 3
Gly Ser Gly Gln Trp Ala Val Gly His Leu Met
1 5 10

<210> ~~SEQ ID NO:~~ 4
<211> ~~LENGTH:~~ 11
<212> ~~TYPE:~~ PRT
<213> ~~ORGANISM:~~ Synthetic

→ <2207

<221> MOD_RES
<222> (1)...(0) delete

<400> ~~SEQ ID NO:~~ 4
Gly Asp Gly Gln Trp Ala Val Gly His Leu Met
1 5 10

<210> ~~SEQ ID NO:~~ 5
<211> ~~LENGTH:~~ 8
<212> ~~TYPE:~~ PRT
<213> ~~ORGANISM:~~ Synthetic

→ <2207

<221> MOD_RES
<222> (1)...(0) delete

<400> ~~SEQ ID NO:~~ 5
Asp Tyr Met Gly Trp Met Asp Phe
1 5

<210> ~~SEQ ID NO:~~ 6
<211> ~~LENGTH:~~ 8
<212> ~~TYPE:~~ PRT
<213> ~~ORGANISM:~~ Synthetic

→ <2207

<221> MOD_RES
<222> (1)...(0) delete

<400> ~~SEQ ID NO:~~ 6
Asp Tyr Nle Gly Trp Nle Asp Phe
1 5

"Nle" is invalid for use in the sequence. Use Xaa and explain in <2207-<2237 section

<210> ~~SEQ ID NO:~~ 7
<211> ~~LENGTH:~~ 8
<212> ~~TYPE:~~ PRT
<213> ~~ORGANISM:~~ Synthetic

→ <2207

<221> MOD_RES
<222> (1)...(0) delete

09/757,332 3

Xaa

<2237> ~~<228>~~ Xff = D-Asp

invalid

~~<400>~~ ~~SEQ ID NO:~~ 7

Xff Tyr Nle Gly Trp Nle Asp Phe

1 invalid 5 invalid

~~<210>~~ ~~SEQ ID NO:~~ 8

~~<211>~~ ~~LENGTH:~~ 8

~~<212>~~ ~~TYPE:~~ PRT

~~<213>~~ ~~ORGANISM:~~ Synthetic

<2207

<2217 MOD_RES

<2227 (1)

<2237 ~~<229>~~ Xaa ~~Xgg~~ = D-Lys

invalid

~~<400>~~ ~~SEQ ID NO:~~ 8

Xgg Pro Arg Arg Pro Tyr Ile Leu

1 5

1) Please consult Sequence Rules for valid format

2) Consult sample Sequence Listing (attached) for valid format

<110> Smith, John; Smithgene Inc.

<120> Example of a Sequence Listing

<130> 01-00001

<140> PCT/EP98/00001
<141> 1998-12-31

<150> US 08/999,999
<151> 1997-10-15

<160> 4

<170> PatentIn version 2.0

<210> 1
<211> 389
<212> DNA
<213> Paramecium sp.

<220>
<221> CDS
<222> (279)...(389)

<300>
<301> Doe, Richard
<302> Isolation and Characterization of a Gene Encoding a Protease from Paramecium sp.
<303> Journal of Genes
<304> 1
<305> 4
<306> 1-7
<307> 1988-06-31
<308> 123456
<309> 1988-06-31

<400> 1

agctgtagtc attcctgtgt cctcttctct ctgggcttct cacccctgcta atcagatctc 60

agggagagtg tcttgaccct cctctgcctt tgcagcttca cagggcaggca ggcaggcagc 120

tgatgtggca attgctggca gtgccacagg ctttttcagcc aggcttaggg tgggttccgc 180

cgcggcgcgg cggccccttct cgcgctcctc tcgcgcctct ctctcgctct cctctcgctc 240

Consult Atkins

Appendix 3, page 2

```
ggacctgatt  aggtgagcag  gaggaggggg  cagttagc      atg gtt tca atg ttc agc  296
                                                  Met Val Ser Met Phe Ser
                                                   1               5

ttg tct ttc aaa tgg cct gga ttt tgt ttg ttt gtt tgt ttg ttc caa  342
Leu Ser Phe Lys Trp Pro Gly Phe Cys Leu Phe Val Cys Leu Phe Gln
            10                  15                  20

tgt ccc aaa gtc ctc ccc tgt cac tca tca ctg cag ccg aat ctt       389
Cys Pro Lys Val Leu Pro Cys His Ser Ser Leu Gln Pro Asn Leu
        25                  30                  35
```

<210> 2
<211> 37
<212> PRT
<213> Paramecium sp.

<400> 2

```
Met Val Ser Met Phe Ser Leu Ser Phe Lys Trp Pro Gly Phe Cys Leu
 1               5                  10                  15

Phe Val Cys Leu Phe Gln Cys Pro Lys Val Leu Pro Cys His Ser Ser
            20                  25                  30

Leu Gln Pro Asn Leu
        35
```

<210> 3
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Designed peptide based on size and polarity to act as a linker between the alpha and beta chains of Protein XYZ.

<400> 3

```
Met Val Asn Leu Glu Pro Met His Thr Glu Ile
 1               5                  10
```

<210> 4
<400> 4
000

[Annex VIII follows]

identifiers and their ass[illegible] applying information as shown in the following table. The numeric identi[illegible]r shall be used only in the "S[illegible]ence Listing." The order and presentation of the items of information in the "Sequence Listing" shall conform to the arrangement given below. Each item of information shall begin on a new line and shall begin with the numeric identifier enclosed in angle brackets as shown. The submission of those items of information designated with an "M" is mandatory. The submission of those items of information designated with an "O" is optional. Numeric identifiers <110> through <170> shall only be set forth at the beginning of the "Sequence Listing." The following table illustrates the numeric identifiers.

Numeric Identifier	Definition	Comments and Format	Mandatory (M) or Optional (O)
<110>	Applicant	Preferably max. of 10 names; one name per line; preferable format: Surname, Other Names and/or Initials	M
<120>	Title of Invention		M
<130>	File Reference	Personal file reference	M, when filed prior to assignment of appl. number
<140>	Current Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if available
<141>	Current Filing Date	Specify as: yyyy-mm-dd	M, if available
<150>	Prior Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if applicable include priority documents under 35 USC 119 and 120
<151>	Prior Application Filing Date	Specify as: yyyy-mm-dd	M, if applicable
<160>	Number of SEQ ID NOs	Count includes total number of SEQ ID NOs	M
<170>	Software	Name of software used to create the Sequence Listing	O
<210>	SEQ ID NO:#:	Response shall be an integer representing the SEQ ID NO shown	M
<211>	Length	Respond with an integer expressing the number of bases or amino acid residues	M

<212>	Type	Whether presented sequence molecule is DNA, RNA, or PRT (protein). If a nucleotide sequence contains both DNA and RNA fragments, the type shall be "DNA." In addition, the combined DNA/RNA molecule shall be further described in the <220> to <223> feature section.	M
<213>	Organism	Scientific name, i.e. Genus/species, Unknown or Artificial Sequence. In addition, the "Unknown" or "Artificial Sequence" organisms shall be further described in the <220> to <223> feature section.	M
<220>	Feature	Leave blank after <220>. <221-223> provide for a description of points of biological significance in the sequence.	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence; if ORGANISM is "Artificial Sequence" or "Unknown"; if molecule is combined DNA/RNA.
<221>	Name/Key	Provide appropriate identifier for feature, preferably from WIPO Standard ST.25 (1998), Appendix 2, Tables 5 and 6	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence
<222>	Location	Specify location within sequence; where appropriate state number of first and last bases/amino acids	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified

		in feature	base was used in a sequence
<223>	Other Information	Other relevant information; four lines maximum	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence; if ORGANISM is "Artificial Sequence" or "Unknown"; if molecule is combined DNA/RNA.
<300>	Publication Information	Leave blank after <300>	O
<301>	Authors	Preferably max of ten named authors of publication; specify one name per line; preferable format: Surname, Other Names and/or Initials	O
<302>	Title		O
<303>	Journal		O
<304>	Volume		O
<305>	Issue		O
<306>	Pages		O
<307>	Date	Journal date on which data published; specify as yyyy-mm-dd, MMM-yyyy or Season-yyyy	O
<308>	Database Accession Number	Accession number assigned by database including database name	O
<309>	Database Entry Date	Date of entry in database; specify as yyyy-mm-dd or MMM-yyyy	O
<310>	Patent Document Number	Document number; for patent-type citations only. Specify as, for example, US 07/999,999	O

<311>	Patent Filing Date	Document filing date, for patent-type citations only; specify as yyyy-mm-dd	O
<312>	Publication Date	Document publication date, for patent-type citations only; specify as yyyy-mm-dd	O
<313>	Relevant Residues	FROM (position) TO (position)	O
<400>	Sequence	SEQ ID NO should follow the numeric identifier and should appear on the line preceding the actual sequence	M

5. Section 1.824 is revised to read as follows:

1.824 Form and format for nucleotide and/or amino acid sequence submissions in computer readable form.

(a) The computer readable form required by 1.821(c) shall meet the following specifications:

(1) The computer readable form shall contain a single "Sequence Listing" as either a diskette, series of diskettes, or other permissible media outlined in paragraph (c) of this section.

(2) The "Sequence Listing" in paragraph (a) (1) of this section shall be submitted in American Standard Code for Information Interchange (ASCII) text. No other formats shall be allowed.

(3) The computer readable form may be created by any means, such as word processors, nucleotide/amino acid sequence editors or other custom computer programs; however, it shall conform to all specifications detailed in this section.

(4) File compression is acceptable when using diskette media, so long as the compressed file is in a self-extracting format that will decompress on one of the systems described in paragraph (b) of this section.

(5) Page numbering shall not appear within the computer readable form version of the "Sequence Listing" file.

(6) All computer readable forms shall have a label permanently affixed thereto on which has been hand-printed or typed: the name of the applicant, the title of the invention, the date on which the data were recorded on the computer readable form, the operating system used, a reference number, and an application serial number and filing date, if known.

(b) Computer readable form submissions must meet these format requirements:

(1) Computer: IBM PC/XT/AT, or compatibles, or Apple Macintosh;

(2) Operating System: MS-DOS, Unix or Macintosh;